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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/552,272	04/19/2000	Li Fang	913.6600CIP	3198

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IP GROUP OF DLA PIPER RUDNICK GRAY CARY US LLP
1650 MARKET ST
SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
EPPS FORD, JANET L	
ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 06/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/552,272	FANG ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,6,10 and 14-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,10 and 14-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3-28-05 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 112

3. Claims 16-57 remain rejected, and claims 58-65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the Official Action mailed 11-19-02.

4. Applicant's arguments filed 3-28-05 have been fully considered but they are not persuasive. Applicants traversed the instant rejection by way of amendment, and on the grounds that the specification includes a full written description for the entire scope of the various claim elements. According to Applicants for a claim drawn to a genus, the written description requirement is satisfied through sufficient description of a representative number of species by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical

properties, or by functional characteristics coupled with a known or disclosed correlation between function and structure, as per the Guidelines for Examination of Patent Applications Under the 35 USC § 112 Written Description Requirement. The examiner agrees with Applicants on this point.

Moreover, Applicants are relying upon the facts set forth in Example 9 of the Written Description Guidelines to support their position that the full scope of compounds encompassed by the instant claims are sufficiently described by the specification as filed.

However, contrary to Applicant's assertions, the facts relied upon in Example 9 of the Written Description Guidelines are distinct from the instant situation. For example, instant claim 16 encompasses nucleic acid sequences that hybridize under low or high stringency conditions. Example 9 of the training materials were limited to those nucleic acid sequence which hybridize under high stringency conditions, not low stringency conditions. Because a high stringency protocol was used for hybridization (per the reasoning set forth in the example), it was concluded that sequences of high structural similarity would have been expected to bind under these conditions. However, in the instant case, based upon the same logic used in Example 9, because nucleic acids, which hybridize under low stringency conditions, are encompassed within the scope of the claims, it is clear that the instant claims encompass sequences with low structural similarity to the reference sequence. Therefore, it is the examiner's position that Applicants have not provided a clear correlation between function and structure as set forth in Example 9. Although Applicants provide functional language to the claims, it clear that the genus of structures which are encompassed by the instant claims (which hybridize under low and high stringency conditions), and require testing in order to identify the recited function, is much

broader than the genus of structures (which hybridize under high stringency conditions) exemplified in the Written Description Guidelines.

Claim 16 is drawn to nucleic acid sequences comprising a fragment that will hybridize under low or high stringency conditions to a reference nucleic acid molecule that is "precisely complementary" to SEQ ID NO: 48, SEQ ID NO: 49 or SEQ ID NO: 50, wherein said first nucleic acid fragment is derived from a first nucleic acid molecule comprising a first cold shock inducible gene having a protein coding region, wherein said first nucleic acid fragment enhances translation of said transcript under conditions that elicit the cold shock response in bacterium. The nucleic acid molecules of the present invention encompass those that hybridize under low stringency conditions to a reference nucleic acid. The skilled artisan would recognize that those sequences which hybridize under low stringency conditions to a reference nucleic acid molecule that is precisely complementary to SEQ ID NO: 48-50, would encompass nucleic acid sequences with a low level of sequence structure similarity to the reference nucleic acid. The genus of nucleic acids encompassed by the instant claims is very broad, and there is no clear correlation between the claimed structures and the recited function. Apart from further experimentation, the skilled artisan would not be able to predict the structures of the full scope of nucleic acid molecules encompassed by the instant claims.

Moreover, in regards to claim 19, Applicants argue that the element of claim 19 defined as the genus of nucleic acid fragments that will hybridize to a reference nucleic acid molecule that is precisely complementary to nucleotides 56-117 of SEQ ID NO: 55 under low or high stringency conditions can also be compared favorably to Example 9 of the Written Description Examples. According to Applicants a person of skill in the art would not expect substantial

variation among species encompassed within the scope of the claimed genus because the hybridization conditions set forth in the claims, would yield structurally similar nucleic acids. Thus, because the specification describes plasmids pMM022, pMM023 and pMM026, which comprise a fragment that will hybridize to nucleotides 56-117 of SEQ ID NO: 55, Applicants conclude that a sufficient number of the genus is disclosed and therefore the full scope of the genus is supported by specification. Contrary to Applicant's assertions, although pMM022, pMM023, and pMM026 comprise a fragment of nucleotides 56-117 of SEQ ID NO: 55, this disclosure is not representative of fragments that will hybridize under low stringency conditions. Moreover, the claims do not require that the recited fragment of nucleotides 56-117 of SEQ ID NO: 55, the claim recites "a fragment," it does not recite SEQ ID N O: 48, 49, SEQ ID NO: 50, nucleotides 56-117 of SEQ ID NO: 55, or a "fragment thereof." The claim merely recites "a fragment."

To the extent that newly added claims 58-65 depend from claims 16-57, newly added claims 58-65 which recite the limitation "a fragment that will hybridize under low or high stringency conditions," are rejected for the reasons given above. Since the claims encompass "a fragment" of unknown length, structure and source, and further wherein said fragment hybridizes under low stringency conditions, the claims are not considered to be sufficiently described by the specification for the reasons given above.

Therefore, although SEQ ID NO: 49, SEQ ID NO: 50, nucleotides 1-11, 56-117, and nucleotides 123-135 of SEQ ID NO: 55 are adequately described by the specification as filed, the specification as filed does not provide an adequate description of the full scope of nucleic acid molecules encompassed by the instant claims.

Claim Rejections - 35 USC § 102

5. Claims 1, 5-15 and 57 remain rejected as being anticipated by Goldstein et al. for the reasons of record set forth in the Official Action mailed 9-13-01; Claims 1, 5-6 and 57 remain rejected as being anticipated by Oppenheim et al. (US Patent No. 5,726,039) or Oppenheim et al. (US Patent No. 5,654,169), for the reasons of record set forth in the Official Action mailed 4-07-04.

Applicant's arguments filed 3-28-05 have been fully considered but they are not persuasive. Applicants traverse the instant claims on the grounds that the additional sequences included in the sequences of Goldstein et al. and Oppenheim et al. would change the basic nature of the claimed isolated nucleic acid molecules. Applicants argued that in the example of a nucleic acid molecule having the sequence of nucleotides 123-135 of SEQ ID NO: 55, the addition of the Shine Delgarno sequence would change the basic nature of this sequence. According to Applicants, the basic nature of nucleotides 123-135 of SEQ ID NO; 55 " is as follows: (1) it is an isolated string of nucleotides that is not incorporate into a gene and is not otherwise capable of transcribing a protein; which, (2) if and when incorporated into a gene and transcribed, will function to enhance translation of the transcript by a certain amount, but will serve no other regulatory or coding function." Furthermore, Applicants argued that any additional sequence added to the molecule having the sequence will remove the construct from the scope of the claim if the additional sequence changes this basic nature.

Contrary to Applicant's assertions, the features relied upon by Applicant's to define the basic nature of the claimed nucleic acid molecules are not recited in the instant claims. If these features are not recited in the claims (or in the specification as filed), it is unclear how one of

skill in the art would recognize that the basic nature of the claimed invention would be influenced by the presence of other nucleic acid structures. Furthermore, in regards to the presence of the Shine Delgarno sequence altering the basic nature of nucleotides 123-135 of SEQ ID NO: 55 by potentially enhancing translation above and beyond the level of nucleotides 123-135, Applicant's arguments are confusing since one of the basic characteristics of the claimed sequence is that it functions to enhance translation. Although, the presence of the Shine Delgarno sequence may potentially enhance translation above and beyond that of the independent sequence, the presence of the additional sequence does not change the ability of nucleotides 123-135 of SEQ ID NO: 55 to enhance translation. Applicant's arguments do not take the place of evidence that the basic nature of the claimed nucleic acid molecules would be altered by the presence of the additional sequences present in the nucleic acid sequences of the cited references. For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." (see MPEP § 2111.03 [R-2]).

Claim 1 recites an isolated nucleic acid molecule that consists essentially of (i.e. comprising) specific sequence structures. However, there is no specific reference to any particular characteristic that is required by these isolated nucleic acid molecules recited in the instant claims, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). According to MPEP § 2111.01 [R-2] "[d]uring examination the

USPTO must give claims their broadest reasonable interpretation. This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification." If Applicants intended that the nucleic acid molecules recited in claim 1 be limited to those having a particular characteristic, Applicants should add that particular characteristic as a limitation in the instant claims, since Applicants are relying on a characteristic that is not immediately obvious to ordinary practitioner, to distinguish the claimed invention from the prior art. Moreover, Applicants argue that none of the sequences recited in claim 1 include a Shine-Delgarno sequence and initiation codon, a protein coding region or a promoter. However, contrary to Applicant's assertions, Applicant's specification (pages 28-29) clearly states, "the expression plasmids *(i.e. vectors)* of the invention may comprise additional sequences known in the art to facilitate the efficient translation of the expressed gene. Such sequences may include a Shine-Delgarno sequence, situated between the 5'UTR sequence and the restriction sites, and/or a DNA fragment encoding a downstream box, situated between the Shine-Delgarno sequence and the restriction sites. The source of the Shine-Delgarno sequence is not especially limited, and may be derived from cold shock proteins or may be from another gene. Such expression plasmids are capable of directing high level expression of a heterologous gene for a prolonged period of time under conditions of physiological stress that elicit a cold shock response of a bacterium." Therefore, Applicant's own specification teach that the presence of a Shine-Delgarno sequence, or other sequences that facilitate the efficient translation of an expressed gene may be comprised within the nucleic acid molecules of the present invention, and do not materially affect the basic characteristics of the claimed invention. Although the sequences recited in the cited references contain additional elements, the sequence

recited in Goldstein and Oppenheim et al. read on the claimed invention since the instant isolated nucleic acid molecules "consist essentially" of nucleotides 1-11 of SEQ ID NO: 55, nucleotides 56-117 of SEQ ID NO: 55, nucleotides 123-135 of SEQ ID NO: 55, SEQ ID NO: 49 or SEQ ID NO: 50, and Applicants have not defined what specified elements would materially affect the basic and novel characteristic(s) of the claimed invention in either the claims or the specification as filed. Absent evidence to the contrary, the nucleic acid structures disclosed in both Goldstein et al. and Oppenheim et al., corresponding to the 5'UTR of the *cspA* cold shock inducible gene of *E. coli,* the *cspA* gene functions as a cold shock inducible gene as recited in the instant claims, and furthermore the 5'UTR of the *cspA* gene comprises (i.e. consists essentially of) the entire sequence of SEQ ID NO: 55 of the instant application. Applicant's arguments do not take the place of evidence that the nucleic acid molecules disclosed by Goldstein et al. and Oppenheim et al. do not read on the isolated nucleic acid molecules of the instant claims.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 1, 5, 6, 10, 14-15, and 57 are rejected under 35 U.S.C. 102(a or e) as being anticipated by Inouye et al. (US Patent No. 5,714,575).

9. It is noted that the phrase "consisting essentially of" recited in claims is interpreted as the transitional phrase "comprising."

Inouye et al. discloses the sequence of SEQ ID NO: 5. This sequence comprises nucleotides 1-11, 56-117 and 123-135 of SEQ ID NO: 55, the underlined sequences of SEQ ID NO: 5 represent the respective sequences:

SEQ ID NO: 5:

A**ACGGUUUGACG**UACAGACCAUUAAAGCAGUGUAGUAAGGCAAGUCCCUUCAAG

AGU**UAUCGUUGAUACCCCUCGUAGUGCACAUUCCUUUAACGCUUCAAAAUCUG**

U AAAGCACGCC-AUAUC**GCCGAAAGGCACA**CUUAAUUAUUAAAGGUAAUACACU

SEQ ID NO: 6 of Inouye et al. comprises the sequence of SEQ ID NO: 49, note the following underlined sequence in SEQ ID NO: 6.

SEQ ID NO: 6:

CGUCGGUUUGAAGAACAGACGAUAUACGAAGUAGUUUACUAAAGCAGUUCUCAU

UUCAGGUGUUAUUCACUUAUUCCUUCUUUGAGUCUCUCCAAUUAAGUACGAAGU

CGUUUCUGUUAUGCAAACCAUUUAU**GCCGAAAGGCUCA**AGUUAAGGAAUGUAGA

Inouye et al. also describes plasmid vector constructs comprising portions of the upstream regulatory sequence of the *cspA* gene linked to a lacZ gene. See col. 9, lines 20-62. In one example is stated that 534 base pairs of the *cspA* upstream regulatory sequence is linked to

the lacZ gene, and was capable of up-regulating the expression of the reporter gene construct at 10°C and 15°C, see Table I.

Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-49, 51, 54-56, and 58-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16, 19, 22, 28, 38, 39-40, 51 and those claims dependent therefrom recite the phrase "derived from," however the specification as filed, nor the claims, provides a precise definition of this phrase such that the skilled artisan would be able to understand the metes and bounds of the claims, for the purpose of avoiding infringement.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Janet L. Epps-Ford, Ph.D.
Patent Examiner
Art Unit 1633

JLE